

Amendments to the Specification

Please replace paragraph [0209] with the following paragraph:

EXAMPLE 3

Particle Size, Particle Density, and Rate of Inhalable Particle Formation of Paroxetine Aerosol

[0209] A solution of 22.0 mg paroxetine in 200 μ L dichloromethane was spread out in a thin layer on the central portion of a 3.5 cm x 7 cm sheet of aluminum foil. The dichloromethane was allowed to evaporate. Assuming a drug density of about 1g/cc, the calculated thickness of the paroxetine thin layer on the 24.5 cm² aluminum solid support, after solvent evaporation, is about 9.0 microns. The aluminum foil was wrapped around a 300 watt halogen tube, which was inserted into a T-shaped glass tube. Both of the openings of the tube were sealed with parafilm, which was punctured with ten needles for flow. The third opening was connected to a 1 liter, 3-neck glass flask. The glass flask was further connected to a large piston capable of drawing 1.1 liters of air through the flask. Alternating current was run through the halogen bulb by application of 90 V using a variac connected to 110 V line power. Within 1 s, an aerosol appeared and was drawn into the 1 L flask by use of the piston, with collection of the aerosol terminated after 6 s. The aerosol was analyzed by connecting the 1 L flask to an eight-stage Andersen non-viable cascade impactor. Results are shown in table 1. MMAD of the collected aerosol was 2.0 microns with a geometric standard deviation of 1.9. Also shown in table 1 is the number of particles collected on the various stages of the cascade impactor, given by the mass collected on the stage divided by the mass of a typical particle trapped on that stage. The mass of a single particle of diameter D is given by the volume of the particle, $\pi D^3/6$, multiplied by the density of the drug (taken to be 1 g/cm³). The inhalable aerosol particle density is the sum of the numbers of particles collected on impactor stages 3 to 8 divided by the collection volume of 1 L, giving an inhalable aerosol particle density of 9.0×10^6 particles/mL. The rate of inhalable aerosol particle formation is the sum of the numbers of particles collected on impactor stages 3 through 8 divided by the formation time of 6 s, giving a rate of inhalable aerosol particle formation of 1.5×10^9 particles/second.

Please replace paragraph [0211] with the following paragraph:

EXAMPLE 4

Drug Mass Density and Rate of Drug Aerosol Formation of Paroxetine Aerosol

[0211] A solution of 19.6 mg paroxetine in 200 μ L dichloromethane was spread out in a thin layer on the central portion of a 3.5 cm x 7 cm sheet of aluminum foil. The dichloromethane was allowed

to evaporate. Assuming a drug density of about 1g/cc, the calculated thickness of the paroxetine thin layer on the 24.5 cm² aluminum solid support, after solvent evaporation, is about 8.0 microns. The aluminum foil was wrapped around a 300 watt halogen tube, which was inserted into a T-shaped glass tube. Both of the openings of the tube were sealed with parafilm, which was punctured with ten needles for flow. The third opening was connected to a 1 liter, 3-neck glass flask. The glass flask was further connected to a large piston capable of drawing 1.1 liters of air through the flask. Alternating current was run through the halogen bulb by application of 90 V using a variac connected to 110 V line power. Within seconds, an aerosol appeared and was drawn into the 1 L flask by use of the piston, with formation of the aerosol terminated after 6 s. The aerosol was allowed to sediment onto the walls of the 1 L flask for approximately 30 minutes. The flask was then extracted with acetonitrile and the extract analyzed by HPLC with detection by light absorption at 225 nm. Comparison with standards containing known amounts of paroxetine revealed that 3.4 mg of > 88% pure paroxetine had been collected in the flask, resulting in an aerosol drug mass density of 3.4 mg/L. The aluminum foil upon which the paroxetine had previously been coated was weighed following the experiment. Of the 19.6 mg originally coated on the aluminum, 7.4 mg of the material was found to have aerosolized in the 6 s time period, implying a rate of drug aerosol formation of 1.2 mg/s.

Please replace paragraph [0212] with the following paragraph:

EXAMPLE 5

Particle Size, Particle Density, and Rate of Inhalable Particle Formation of Mirtazepine Aerosol

[0212] A solution of 18.7 mg mirtazepine in 200 µL dichloromethane was spread out in a thin layer on the central portion of a 3.5 cm x 7 cm sheet of aluminum foil. The dichloromethane was allowed to evaporate. Assuming a drug density of about 1g/cc, the calculated thickness of the mirtazepine thin layer on the 24.5 cm² aluminum solid support, after solvent evaporation, is about 7.6 microns. The aluminum foil was wrapped around a 300 watt halogen tube, which was inserted into a T-shaped glass tube. Both of the openings of the tube were sealed with parafilm, which was punctured with ten needles for air flow. The third opening was connected to a 1 liter, 3-neck glass flask. The glass flask was further connected to a large piston capable of drawing 1.1 liters of air through the flask. Alternating current was run through the halogen bulb by application of 90 V using a variac connected to 110 V line power. Within 1 s, an aerosol appeared and was drawn into the 1 L flask by use of the piston, with collection of the aerosol terminated after 6 s. The aerosol was analyzed by connecting the 1 L flask to an eight-stage Andersen non-viable cascade impactor. Results are shown in table 1. MMAD of the collected aerosol

was 1.2 microns with a geometric standard deviation of 2.2. Also shown in table 1 is the number of particles collected on the various stages of the cascade impactor, given by the mass collected on the stage divided by the mass of a typical particle trapped on that stage. The mass of a single particle of diameter D is given by the volume of the particle, $\pi D^3/6$, multiplied by the density of the drug (taken to be 1 g/cm^3). The inhalable aerosol particle density is the sum of the numbers of particles collected on impactor stages 3 to 8 divided by the collection volume of 1 L, giving an inhalable aerosol particle density of 5.6×10^7 particles/mL. The rate of inhalable aerosol particle formation is the sum of the numbers of particles collected on impactor stages 3 through 8 divided by the formation time of 6 s, giving a rate of inhalable aerosol particle formation of 9.3×10^6 particles/second.

Please replace paragraph [0214] with the following paragraph:

EXAMPLE 6

Drug Mass Density and Rate of Drug Aerosol Formation of Mirtazepine Aerosol

[0214] A solution of 20.7 mg mirtazepine in 200 μL dichloromethane was spread out in a thin layer on the central portion of a 3.5 cm x 7 cm sheet of aluminum foil. The dichloromethane was allowed to evaporate. Assuming a drug density of about 1g/cc, the calculated thickness of the mirtazepine thin layer on the 24.5 cm² aluminum solid support, after solvent evaporation, is about 8.4 microns. The aluminum foil was wrapped around a 300 watt halogen tube, which was inserted into a T-shaped glass tube. Both of the openings of the tube were sealed with parafilm, which was punctured with ten needles for air flow. The third opening was connected to a 1 liter, 3-neck glass flask. The glass flask was further connected to a large piston capable of drawing 1.1 liters of air through the flask. Alternating current was run through the halogen bulb by application of 90 V using a variac connected to 110 V line power. Within seconds, an aerosol appeared and was drawn into the 1 L flask by use of the piston, with formation of the aerosol terminated after 6 s. The aerosol was allowed to sediment onto the walls of the 1 L flask for approximately 30 minutes. The flask was then extracted with acetonitrile and the extract analyzed by HPLC with detection by light absorption at 225 nm. Comparison with standards containing known amounts of mirtazepine revealed that 10.65 mg of > 99% pure mirtazepine had been collected in the flask, resulting in an aerosol drug mass density of 10.65 mg/L. The aluminum foil upon which the mirtazepine had previously been coated was weighed following the experiment. Of the 20.7 mg originally coated on the aluminum, 18.7 mg of the material was found to have aerosolized in the 6 s time period, implying a rate of drug aerosol formation of 3.1 mg/s.